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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/884,629	06/19/2001	Peter H. St. George-Hyslop	1034/1J800US1	3866

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EXAMINER	
HAMA, JOANNE	

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1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/884,629	ST. GEORGE-HYSLOP ET AL.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-24,27-35,38,39* is/are pending in the application.

4a) Of the above claim(s) *8-23 and 29-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-7,24,27,28,38 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the Non-Final Action of December 18, 2006 on June 18, 2007. Claims 2, 4, 25, 26, 36, 37 are cancelled. Claims 1, 5-7, 24, 27, 28 are amended. Claims 8-23, 29-35 are withdrawn. Claims 38 and 39 are new.

Claims 1, 3, 5-7, 24, 27, 28, 38, 39 are under consideration.

This application contains claims 8-23, 29-35 drawn to an invention nonelected with traverse in the reply filed on February 21, 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawn Rejection

35 U.S.C. § 101

Applicant's arguments, see pages 18-22, filed June 18, 2007, with respect to the rejection of claims 1, 3-7, 24, 26-28, 36, 37 have been fully considered and are persuasive. Applicant indicates that the important feature of a relevant animal model is whether the amyloid pathology of the model resembles that of human Alzheimer's disease and not whether the combination of mutations in the animal is identical to any particular human case of human disease. The application discloses on page 10, lines 4-14 that the claimed mouse displays abnormal Abeta deposition similar to that seen in human patients with Alzheimer's disease (Applicant's emphasis, Applicant's response, pages 20-21). In response, this is persuasive and the rejection as it applies to this issue is withdrawn. Applicant also indicates that there is utility for the nucleic acid sequence

and vector because the claimed mice have utility (Applicant's response, page 21). In response, this is persuasive and the issue as it applies to this issue is withdrawn. The rejection of claims 1, 3, 5-7, 24, 27, 28 has been withdrawn. It is noted that the rejection of claims 4, 26, 36, 37 is withdrawn as the claims are cancelled.

35 U.S.C. § 112, 2nd parag.

Applicant's arguments, see pages 26-27 of Applicant's response, filed June 18, 2007, with respect to the rejection of claims 6, 24, 26, 37 have been fully considered and are persuasive. With regard to claim 6 having no antecedent for "the animal" of claim 1, Applicant indicates that claim 6 has been amended to "mouse". With regard to claim 24, step d, appearing to lack the word, "its," Applicant indicates the claim 24 has been amended to include "its." Claims 26 and 37 depended on claim 24 and had thus been rejected. The rejection of claims 6 and 24 has been withdrawn. It is noted that the rejection of claims 26 and 37 are withdrawn as the claims have been cancelled.

New Objection/Rejections

Claim Objection

Claims 38 and 39 are newly objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 38 depends on claim 1; claim 39 depends on claim 24. Claims 1 and 24 already have

the limitation of the mouse's genetic background and it appears that claims 38 and 39 are redundant.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5-7, 24, 28, 38, 39 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. The claims are drawn to use of a cos.Tet promoter. However, nothing in the specification teaches what a cos.Tet promoter is. The closest reference to "cos.Tet" is that it is an expression construct (specification, page 4, 4th parag.). However, an expression construct is not a promoter.

Claims 1, 3, 5-7, 24, 28, 38, 39 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement for a claimed genus is satisfied by sufficient description of a representative number of species by actual reduction to practice and by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicant were in possession of the claimed genus.

The final Written Description Examination guidelines that were published on January 5, 2001 (66 FR 1099; available at http://www.uspto.gov/web/menu/current.html#register).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

With regard to the claims being drawn to the use of a cos.Tet promoter, nothing in the art or specification provides any guidance as to what a cos.Tet promoter is. While claim 1, as written, indicates that the promoter drives expression in the central nervous system and has neuronal expression, the specification and art provide no structural guidance of the promoter such that it can be identified. The claimed invention as a whole is not adequately described if the claims require essential or critical elements

which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). In the instant case, while the specification refers to a cos.Tet expression construct (specification, page 4, 4th parag.), the specification provides no guidance as to what structure a cos.Tet promoter has such that an artisan could obtain cos.Tet promoters, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, no cos.Tet promoters meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the

written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1, 3, 5-7, 24, 28, 38, 39 remain rejected in modified form under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

1) a C3H x C57 mouse whose genome comprises a transgene comprising a nucleotide sequence operably linked to a Syrian hamster prion protein gene promoter and encoding a heterologous human amyloid precursor protein $695_{Sw, Ind}$ ($APP695_{Sw, Ind}$) wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine, wherein said promoter directs central nervous system or neuronal expression of said transgene and wherein said mouse displays abnormal Aβ deposition in its central nervous system and

2) a method of producing a C3H x C57 mouse that displays abnormal Aβ deposition in its central nervous system comprising:

a) introducing into a fertilized oocyte of said mouse, a transgene comprising a nucleotide sequence operably linked to a Syrian hamster prion protein gene promoter and encoding a heterologous human amyloid precursor protein $695_{Sw, Ind}$ ($APP695_{Sw, Ind}$) wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine, wherein said promoter directs central nervous system or neuronal expression of said transgene,

b) transplanting said fertilized oocyte into a pseudopregnant mouse,

c) allowing said fertilized oocyte to develop into a live born offspring, and

d) selecting an offspring where its genome comprises a nucleotide sequence operably linked to a Syrian hamster prion protein gene promoter and encoding a heterologous human amyloid precursor protein $695_{Sw, Ind}$ ($APP695_{Sw, Ind}$), wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine, wherein the transgene is expressed,

does not reasonably provide enablement for

1) a C3H x C57 mouse whose genome comprises a transgene comprising a nucleotide sequence operably linked to a cos.tet promoter and encoding a heterologous human amyloid precursor protein $695_{Sw, Ind}$ ($APP695_{Sw, Ind}$) wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine, wherein said promoter directs central nervous system or neuronal expression of said transgene and wherein said mouse displays abnormal Aβ deposition in its central nervous system.

2) a method of producing a C3H x C57 mouse that displays abnormal Aβ deposition in its central nervous system comprising:

a) introducing into a fertilized oocyte of said mouse, a transgene comprising a nucleotide sequence operably linked to a cos.tet promoter and encoding a heterologous human amyloid precursor protein $695_{Sw, Ind}$ ($APP695_{Sw, Ind}$) wherein the

lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine, wherein said promoter directs central nervous system or neuronal expression of said transgene,

b) transplanting said fertilized oocyte into a pseudopregnant mouse,

c) allowing said fertilized oocyte to develop into a live born offspring, and

d) selecting an offspring where its genome comprises a nucleotide sequence operably linked to a Syrian hamster prion protein gene promoter and encoding a heterologous human amyloid precursor protein $695_{Sw, Ind}$ ($APP695_{Sw, Ind}$) wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine, wherein the transgene is expressed.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's amendments raise new issues of rejection. Response to Applicant's rebuttals of June 18, 2007 is provided following the new issues of rejection.

The claims are drawn to the use of a cos.Tet promoter. However, looking through the specification and the art, nothing in the specification or the art teaches what a cos.Tet promoter is. The specification teaches that the cosTet expression vector contains the Syrian hamster prion protein gene promoter (specification, page 4, 4th

parag.); however, nothing in the specification or the art indicates what a cos.Tet promoter is. As such, the claims are rejected.

Claim 7 indicates that the claimed mouse has a C3H xC57 mouse as its ancestor. This means that claim 7 encompasses descendant mice that have an FVB/N genetic background. However, according to the specification, mice containing an FBV/N genetic background are prone to premature death in early adult life and the specification does not provide guidance as to how to use mice with this genetic background. As such, claim 7 is rejected.

Applicant's arguments, see pages 22-26 of Applicant's response, filed June 18, 2007, with respect to the rejection of claims 1, 3-7, 24, 26-28, 36, 37 have been fully considered and are persuasive in part.

Applicant indicates that claim 1 has been amended to recite a C3H xC57 mouse whose genome comprises a human $APP695_{Sw, Ind}$ transgene operably linked to a cos.Tet promoter wherein said transgenic mouse displays abnormal Abeta deposition in its central nervous system. Claim 24, as amended, recites a method for producing such mouse (Applicant's response, page 25). This is found persuasive in part and the rejection involving the issues of the animal source of APP695 and the mutations associated with APP695, and the claimed mouse exhibiting a phenotype is withdrawn. As for the issue of the promoter and the mouse's genetic background, the specification does not provide guidance on how to obtain a cos.Tet promoter (see above) and mice of any genetic background and the claims are thus rejected for use of this promoter and any genetic background.

It is noted that the rejection of claims 4, 26, 36, 37 are withdrawn as the claims are cancelled. It is also noted that the rejection of claim 27 is withdrawn as Applicant indicates that because the claimed mice have an enabled use, the nucleic acid sequence used to make them has an enabled use.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 7, 38, 39 is newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 7, 38 recite the limitation "transgenic mouse" in claim 1. There is insufficient antecedent basis for this limitation in the claim. Similarly, claim 39 refers to the transgenic mouse of claim 24. However, there is insufficient antecedent basis for this limitation in the claim.

Claim 39 is unclear because the claim is drawn to a transgenic mouse, and the claim upon which it depends, claim 24, is a method claim. Claim 39 might be amended to read, "the method of claim 24, wherein the mouse....".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 27 remains rejected under 35 U.S.C. 102(b) as being anticipated by Hsia et al., 1999, PNSA, USA, 96: 3228-3233, previously cited, as evidenced by Jin et al., 2004, PNAS, USA, 101, 13363-13367, previously cited, and Selkoe, 2002, Science, 298: 789-791, previously cited.

Applicant's arguments, see pages 27-29 of Applicant's response, filed June 18, 2007, with respect to the rejection of claims 1, 4-7, 24, 27, 28, 36, 37 have been fully considered and are persuasive in part.

Applicant indicates that claim 1 has been amended and indicates that the mouse in claims 1 has a particular genetic background (C3H x C57) and that the cos.Tet promoter drives expression of the transgene of interest. This was not taught by Hsia et al. (Applicant's response, page 28, 2nd parag.). As such, the rejection of claims 1, 5-7, 24, 28 has been withdrawn.

However, Hsia et al. anticipate claim 27, drawn to a nucleotide sequence encoding human amyloid precursor protein 695, wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine, as Hsia et al. teach a PDGF-$APP_{Sw,Ind}$ construct (Hsia, et al., page 3228, 2nd col. under "Transgenic Mouse Lines"). Note that $APP_{Sw,Ind}$ comprise the required mutations (e.g. see Jin et al., 2004, page 13363, 2nd col., 3rd parag.). As such, the rejection of claim 27 remains.

It is noted that the rejection of claims 4, 36, 37 is withdrawn as the claims are cancelled.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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/Anne Marie S. Wehbé/
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